REMARKS

This amendment is filed in response to the Office Action mailed May 17, 2001 (Paper No. 13). Claims 10-16 are pending and the species of SEQ ID NO:4 was elected. Claim 10 has been cancelled and claims 11-16 have been amended to recite the elected species. The title has been amended as suggested by the Examiner. The application cited at page 29, line 13 has not issued as a patent, so this section has not been updated. No new matter is added by these amendments.

The Examiner noted that Reference 3 on the IDS PTO 1449 filed on November 20, 2000 was not considered. A new IDS and statement of relevance are filed herewith.

Claims 10-16 were rejected under 35 U.S.C. § 101 because the claimed invention allegedly is not supported by a credible, specific and substantial asserted utility or a well-established utility. The Examiner reviewed six asserted utilities for the polypeptide of SEQ ID NO:4, and found that none of them meet the statutory requirement. Applicants respectfully traverse this rejection.

The Examiner states that several utilities are implied from the specification, as listed at page 5, lines 1-9 of the Office Action. Applicants submit that one utility of the invention can be found in the fact that applicants have identified a human homologue of rat plasmolipin, and that the Patent Office and the art have recognized a specific, credible and substantial utility for this protein, as evidenced by the discussion below and the attached exhibits.

U.S. Patent No. 5,843,714, issued December 1, 1998, discloses a novel human proteolipid which, according to the patentee, has homology to rat plasmolipin, specifically, 43% sequence identity (column 4, lines 61-64). This patent fails to meet any of the six possible utility requirements that the Examiner has applied to the present application. However, (under previous utility guidelines) the PTO did issue a patent that identified the new protein as a human plasmolipin.

A close examination of Figure 2 of the '714 patent shows that there are only 57 amino acids in common between the claimed PLHu sequence and rat plasmolipin (referred to as GI 1346732). In contrast, of the 158 amino acids shown for rat plasmolipin, 140 are common to applicants' plasmolipin-like protein, SEQ ID NO:4. Applicants submit that their claimed protein

has a greater claim to homology with rat plasmolipin, and to shared functional attributes, than does the protein of the '714 patent.

The functional attributes that provide the specific, substantial, and credible utility for applicants' claimed sequence are discussed below.

1. Credible utility.

According to the Utility Examination Guidelines (Fed. Reg. Vol. 66 No. 4, 1092, 1098 (January 5, 2001)),

> Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record...

Suitable evidence of record includes patents or printed publications, specific examples of which are discussed below. An applicant need only provide one credible assertion of specific and substantial utility. One credible assertion put forth in the application is that the claimed polynucleotide encodes a human homologue of rat plasmolipin. As discussed above, one of ordinary skill in the art previously identified a protein having only 43% sequence identify with rat plasmolipin (47 amino acids), and referred to it as "human plasmolipin PLHu." (U.S. Patent No. 5,843,714.) It is therefore credible that a protein having not 57 but 140 amino acids in common with the *same* referenced rat plasmolipin sequence can correctly be designated as a human plasmolipin. A copy of the '714 patent is submitted herewith. Applicants have found that the rat plasmolipin sequence shares 140/157 amino acids with the region of applicants' SEQ ID NO:4 between amino acids 27 and 181.

Applicants submit therefore that the statement in the specification regarding the homology with rat plasmolipin (page 30, lines 3-6) represents a credible assertion of utility.

2. Specific and substantial utility.

The guidelines cited above state that this requirement precludes "throw-away," "insubstantial," or "non-specific" utilities. Applicants submit that the claimed invention satisfies this requirement. Plasmolipin is a protein that is well-recognized in the art as playing a role in ion transport in cell membranes, and is involved in myelination, particularly during development

of sciatic nerve and brain, and after sciatic nerve injury. (Gillen, C. et al., *Eur. J. Neurosci.* (1996) *8*:405-414, a copy of which is attached.)

The claimed invention therefore has a utility that is *specific* to a particular class of proteins (plasmolipins), and that is *substantial*, because these proteins play a role in myelination. Thus, they are removed from the general category of amino acid sequences of unidentified function.

In compliance with the Utility Guidelines, the Examiner has imposed a rejection under 35 U.S.C. § 101, and the burden has shifted to applicants to come forward with evidence that (1) identifies a specific and substantial utility for the claimed invention and (2) shows that this utility was established at the time of filing. Applicants submit that they have met this burden.

The accompanying Gillen, C. et al. publication shows that rat plasmolipin mRNA levels were altered during development of sciatic nerve and brain, and after sciatic nerve injury. This paper was published before applicants' filing date of June 30, 1999. Applicants cited the similarity of the claimed sequence to rat plasmolipin in their specification, and this is further elucidated by the amino acid sequence comparison discussed above in reference to the '714 patent.

Applicants' specification discloses that crushed nerves undergoing regeneration displayed increased transcript levels of plasmolipin (page 5, lines 22-23). Thus, the specification clearly supports a specific utility for the polynucleotide of SEQ ID NO:3, namely, as a marker for nerve regeneration. In view of the biological and pathological importance of this process, one of skill would recognize this to be a *substantial* utility, that is *specific* to the claimed sequence. The credibility of this utility is supported by the recognition by those skilled in the art that plasmolipin levels correlate with nerve injury.

In view of the arguments and evidence submitted herewith, applicants submit that they have successfully rebutted the Examiner's assertion of a *prima facie* lack of utility, and request withdrawal of this rejection.

Claims 10-16 were rejected under 35 U.S.C. § 112, first paragraph, as one skilled in the art allegedly would not know how to use the claimed invention in view of the asserted lack of utility.

In view of the arguments above related to utility of the protein, applicants submit that this rejection may be withdrawn. The Examiner also reviewed the current enablement requirements and concluded that the specification does not teach one of skill how to make or use polypeptide variants of SEQ ID NO:4. Without acquiescing to the ground of rejection, applicants have cancelled claim 10.

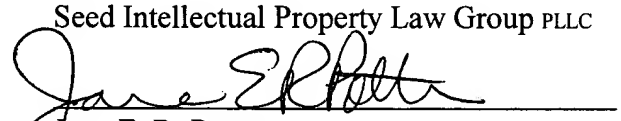
Claim 10 was rejected under 35 U.S.C. § 112, first paragraph, as the specification allegedly does not teach functional or structural characteristics of the polypeptides of claim 10. Without acquiescing to the ground of rejection, applicants have cancelled claim 10.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version With Markings to Show Changes Made.**"

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

Seed Intellectual Property Law Group PLLC



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Enclosures: U.S. Patent No. 5,843,714
Gillen, *European J. of Neuroscience 8*:405-414

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Title:

The title has been changed as follows:

HUMAN CHROMOSOME [15 AND]16 [BARDET-BIEDL SYNDROME POLYNUCLEOTIDES AND POLYPEPTIDES AND METHODS OF USE] PLASMOLIPIN-LIKE POLYPEPTIDE

In the Claims:

11. (Amended) An isolated polypeptide wherein, except for at least one conservative amino acid substitution, said polypeptide has an amino acid sequence selected from the group consisting of:

[(a) amino acids from about 1 to about 254 of SEQ ID NO:2;

(b) amino acids from about 2 to about 254 of SEQ ID NO:2;]

([c]a) amino acids from about 1 to about 218 of SEQ ID NO:4; and

([d]b) amino acids from about 2 to about 218 of SEQ ID NO:4[;].

[(e) amino acids from about 1 to about 297 of SEQ ID NO:6;

(f) amino acids from about 2 to about 297 of SEQ ID NO:6;

(g) amino acids from about 1 to about 513 of SEQ ID NO:9;

(h) amino acids from about 2 to about 513 of SEQ ID NO:9.]

12. (Amended) An isolated polypeptide comprising amino selected from the group consisting of:

[(a) amino acids from about 1 to about 254 of SEQ ID NO:2;

(b) amino acids from about 2 to about 254 of SEQ ID NO:2;]

([c]a) amino acids from about 1 to about 218 of SEQ ID NO:4; and

([d]b) amino acids from about 2 to about 218 of SEQ ID NO:4[;].

[(e) amino acids from about 1 to about 297 of SEQ ID NO:6;

(f) amino acids from about 2 to about 297of SEQ ID NO:6;

(g) amino acids from about 1 to about 513 of SEQ ID NO:9;

(h) amino acids from about 2 to about 513 of SEQ ID NO:9.]

13. (Amended) An epitope-bearing portion of a polypeptide [selected from the group consisting] of [SEQ ID NO:2,] SEQ ID NO:4[, SEQ ID NO:6, and SEQ ID NO:9].

14. (Amended) The epitope-bearing portion of claim 13, which comprises between about 10 and 100 contiguous amino acids of [SEQ ID NO:2,] SEQ ID NO:4[, SEQ ID NO:6, or SEQ ID NO:9].

15. (Amended) The epitope-bearing portion of claim 14, which comprises between about 12 and 50 contiguous amino acids of [SEQ ID NO:2,] SEQ ID NO:4[, SEQ ID NO:6, or SEQ ID NO:9].

16. (Amended) The epitope-bearing portion of claim 14, which comprises between about 15 and 25 contiguous amino acids of [SEQ ID NO:2,] SEQ ID NO:4[, SEQ ID NO:6, or SEQ ID NO:9].